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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,743	12/12/2000	Wei-min Liu	3298.1	7518

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EXAMINER

ALLEN, MARIANNE P

ART UNIT PAPER NUMBER

1631

DATE MAILED: 07/24/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/735,743

Applicant(s)

LIU ET AL.

Examiner

Marianne P. Allen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 May 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11-21, 23-34, 36-47, 49-59, 61-72, 74-85, 87-97 and 99-103 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11-21, 23-34, 36-47, 49-59, 61-72, 74-85, 87-97 and 99-103 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☒ The proposed drawing correction filed on 09 May 2003 is: a) ☐ approved b) ☒ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>6</u> . | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Claims 10, 22, 35, 48, 60, 73, 86, and 98 have been cancelled. Claim 103 has been newly added.

Applicant's arguments filed 5/9/03 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant is advised that the marked up copy of the claims as well as the appended current version of the whole claim set do not correspond to the claims that are pending. Compare at least claims 100, 101, and 102 among the three versions. Applicant is reminded that the clean copy of the amended claims and the originally filed claims are the binding versions and are the version under examination.

Specification/Drawings

The proposed drawing correction to Figure 6, filed on 5/9/03 has been disapproved because they introduce new matter into the drawings. 37 CFR 1.121(f) states that no amendment may introduce new matter into the disclosure of an application.

The amendment filed 5/9/03 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention.

The amendment filed 5/9/03 changes various formulas throughout the specification, figure 6, and claims. The only explanation provided is that typographical errors were corrected. While various inconsistencies in the specification, figures, and claims were pointed out in the

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prior Office action, a typographical error is an error where one of ordinary skill in the art recognizes that an error is present as well as recognizing what its correction should be. The fact that the examiner identified inconsistencies is not recognition of what the correct formulas should have been based upon the disclosure, particularly when the formulas are repeated several times with the same or differing notation.

Applicant is required to cancel the new matter in the reply to this Office Action or provide a clear explanation supporting the changes to formulas. Failure to provide such an explanation is considered to be an admission that the originally filed specification is fatally defective.

Claim Rejections - 35 USC § 112

Claims 1-9, 11-21, 23-34, 36-47, 49-59, 61-72, 74-85, 87-97, and 99-103 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention as well as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a new matter and enablement rejection.

Applicant has amended formulas in the specification, figures, and claims without providing basis for these changes. See objection to figures and specification above.

Claim 103 has been newly introduced. No basis has been pointed to for this claim and none is apparent.

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The enablement portion of the rejection is maintained essentially for reasons of record and applied to claim 103 for the same reasons as summarized below.

Claims 1, 26, 39, 64, 77, and 91-103 require an unspecified test statistic. While particular test statistics are disclosed, the specification does not provide guidance on selecting or developing other test statistics for use in the claimed method nor the associated threshold values. It would require undue experimentation for one of ordinary skill in the art to derive additional test statistics that would be appropriate for use in the claimed method. Applicant argues that it is within the skill of the art to develop additional suitable statistics. This assertion is unsupported by any evidence that such developments would have been routine and not require inventive skill, judgment, and decision making on the part of the practitioner. There is no evidence of record that test statistics (including the appropriate threshold values) for intensity differences between perfect match and mismatch probes suitable for determining whether a transcript is present or absent were routinely developed and validated. Given that the particular test statistics and associated threshold values disclosed are applicant's inventive concept, the examiner maintains that this falls outside the bounds of routine experimentation. The specification does not provide guidance or suggestions for other test statistics, particularly those that would have the thresholds and significance levels set forth in the dependent claims.

Claims 1-2, 6-9, 11-12, 14-15, 26-27, 31-34, 36-40, 44-47, 49-53, 56-69, 61-65, 69-72, 74-78, 82-85, 87-91, and 93-103 require a threshold value without reciting how it is determined or its value. Claims 4 and 5 recite two different equations for calculating the threshold value. It appears that τ_1 is the threshold value but the claims do not make this clear. Nevertheless, the specification does not disclose the value of the constant, c_1 , nor does it provide guidance on how

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to determine or calculate the constant. Page 24 gives another equation for threshold; however, several of the variables are undefined. The examples provide particular threshold values for the particular experiments performed but does not disclose how they were selected or computed. In particular, page 40 discloses the parameter with respect to Equation (3c) where $c''_1 = 1.2$. Note that this equation and constant notation do not appear to be present in the specification.

Likewise, claim 26 requires a threshold. Claims 27, 29, and 30 disclose equations for calculating the threshold for the aforementioned testing statistic; however, the specification does not disclose the value of the constant, nor does it provide guidance on how to determine or calculate the constant. With the exception of where the threshold is zero or specifically provided, one of ordinary skill in the art would not know what threshold to use or how to determine it, particularly for an undefined test statistic. Applicant has not explained why the specification would have provided guidance to one of ordinary skill in the art beyond the specifically disclosed threshold values for the particular test statistics disclosed.

The claims require indicating whether a transcript is present based upon a p -value. The claims are considered to be directed to determining the correct answer with respect to presence or absence and eliminating false positives and false negatives. As such, the parameters that would provide such a result must be taught and the claims must contain limitations that would lead to this result. Many of the claims do not require a particular significance level for the p -value to make this determination.

Claims 14-21, 23-25, 39-47, 49-51, 52-59, 61-72, and 74-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites a testing statistic $median((PM_i - MM_i)/(PM + MM_i))$. This still appears to be an erroneous formula that is inconsistent with similar formulas in the specification. Note the lack of a subscript “i” in the denominator for PM. Applicant is again cautioned against introducing new matter. See also claim 90.

Claim 39 remains confusing for reasons of record. Contrary to applicant’s arguments, the claim does not clearly require that the code is stored on the computer readable media. “For” is considered to be an intended use and not a requirement for storage. Applicant did not respond to the portion of the rejection with respect to whether the software product of the preamble is an integrated product where the results of one program code are used as input for the next computer program code or whether these are three discrete pieces of software. See also claim 64.

Claim Rejections - 35 USC § 103

Claims 1, 39, and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (1996) in view of either Hogg et al. or Hollander et al.

This rejection is maintained for reasons of record.

Applicant argues that the Office action fails to point out the basis for the assertion that one of ordinary skill in the art would have been aware that hybridization data from nucleic acid arrays could be used in nonparametric statistical tests. A parametric test assumes the data was from a population that follows a Gaussian or normal distribution. A nonparametric test does not

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assume a particular distribution of data. Using nonparametric statistics would have been well known in the nucleic acid arts and expression analysis with respect to differences in signal intensity. See at least Lynch et al. (U.S. Patent No. 5,988,139 at column 9, lines 44-51), Chartier-Harlin et al. (U.S. Patent No. 6,391,553 at column 8, lines 38-53), Kargman et al. (U.S. Patent No. 6,593,361 at column 15, line 67, through column 16, line 30) as evidence that those of ordinary skill in the art would have understood the applicability of nonparametric statistics, including Wilcoxon's signed rank test, in this area of technology.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 703-308-0666. The examiner can normally be reached on Monday-Friday, 8:30 am - 2:30 pm.

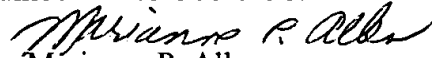
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Marianne P. Allen
Primary Examiner
Art Unit 1631

mpa
July 23, 2003